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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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*Ex parte* BYUNG SOOK MOON, MARTIN JONES,  
and JOHNNY VALDEZ

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Appeal 2010-002958  
Application 10/672,266  
Technology Center 1600

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Before LORA M. GREEN, MELANIE L. McCOLLUM, and  
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a lyophilized bead for use in amplification. The Examiner rejected the claims as lacking description and as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

*Statement of the Case*

*The Claims*

Claims 1-10, 12, 45-48, 50-53, 63, and 64 are on appeal.

Claim 1 is representative and reads as follows:

1. A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, said lyophilized bead being substantially spherical in shape and comprising:  
a thermally stable enzyme; and  
mannitol;  
wherein said lyophilized bead has a weight percentage of said mannitol of between about 53% and about 75% (w/w).

*The issues*

- A. The Examiner rejected claims 1-10, 12, 45-48, and 50-53 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement (Ans. 3).
- B. The Examiner rejected claims 1-7, 10, 12, 45-48, 52, 53, 63, and 64 under 35 U.S.C. § 103(a) as obvious over Park<sup>1</sup> and Trembl<sup>2</sup> (Ans. 4-9).
- C. The Examiner rejected claims 8 and 50 under 35 U.S.C. § 103(a) as obvious over Park, Trembl, and Kellogg<sup>3</sup> (Ans. 9-10).
- D. The Examiner rejected claims 9 and 51 under 35 U.S.C. § 103(a) as obvious over Park, Trembl, and Shively<sup>4</sup> (Ans. 10-11).

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<sup>1</sup> Park et al., US 5,861,251, Jan. 19, 1999.

<sup>2</sup> Trembl et al., US 5,763,157, Jun. 9, 1998.

<sup>3</sup> Kellogg et al., *TaqStart Antibody<sup>TM</sup>: "Hot Start" PCR Facilitated by a Neutralizing Monoclonal Antibody Directed Against Taq DNA Polymerase*, 16 BiOTECHNIQUES 1134-1137 (1994).

A. 35 U.S.C. § 112, first paragraph, written description

The Examiner finds that “[r]egarding claims 1 and 45 applicant has added the limitation ‘substantially spherical’. [The] Examiner could not find even a single instance in the specification where [the] term substantial or substantially was used in context of the spherical lyophilized beads” (Ans. 3).

Appellants “submit that there is sufficient written description support for the limitation ‘substantially spherical’ and that it is clear to the reader of the instant claims that Applicants had possession of the invention at the time of filing the application” (App. Br. 5). Appellants contend that “the definition of ‘bead’ at page 7, lines 10-17 provides that ‘[a] bead can have a spherical as well as a nearly spherical, e.g., elliptical, shape’” (*id.*).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s finding that claim 1 fails to comply with the written description requirement as incorporating new matter?

*Findings of Fact*

1. The Specification teaches that a “‘bead’, as used herein, refers to a small, often round piece of material. A bead can have a spherical as well as a nearly spherical, e.g., elliptical shape” (Spec. 7, ll. 10-11).

2. The Specification teaches that “[e]xemplary shapes include spherical, near spherical, elliptical or round structures” (Spec. 10, ll. 26-27).

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<sup>4</sup>Shively, *Real-Time PCR Assay for Quantitative Mismatch Detection*, 34 BIO TECHNIQUES 498-504 (2003).

*Principles of Law*

“[T]he written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement” *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010).

“[I]t is the specification itself that must demonstrate possession. And while the description requirement does not demand any particular form of disclosure, ... or that the specification recite the claimed invention *in haec verba*, a description that merely renders the invention obvious does not satisfy the requirement” *Id.* (citations omitted).

*Analysis*

We agree with Appellants that the phrase “substantially spherical” is simply a change in nomenclature from the disclosed “nearly spherical” description given in the Specification (FF 1-2). The Examiner has not provided any reason why substitution of the word “substantially” for “nearly” lacks descriptive support in the Specification.

*Conclusion of Law*

The evidence of record does not support the Examiner’s finding that claims 1 and 45 fail to comply with the written description requirement as incorporating new matter.

*B. 35 U.S.C. § 103(a) over Park and Trembl*

The Examiner finds that Park teaches a “lyophilized reagent comprising: a thermally stable enzyme” (Ans. 5). The Examiner finds that Park teaches the use of “mannitol as a stabilizer. Mannitol is part of their

preferred stabilizers falling in the group of polyols composed of glycerol, glucose, mannitol, galacitol, glucitol and sorbitol” (Ans. 5).

The Examiner finds that Trembl teaches beads which “are composed of a high molecular weight synthetic carbohydrate polymer and a second carbohydrate. Examples of second carbohydrate used by Trembl et al. includes polyols such as sorbitol” (*id.* at 6). The Examiner finds that the “range disclosed by Trembl et al. would be about 45% (w/w)” (*id.*).

Appellants contend that “Trembl teaches away from the present invention by disclosing compositions having at most 40% (w/w) of a carbohydrate, a carbohydrate composition that is substantially *below* the lowest claimed mannitol composition of 53% (w/w)” (App. Br. 6).

Appellants contend that, according to the Jones Declaration<sup>5</sup>, the “substantially spherical nature of the beads is inherent to the use of mannitol in the claimed range. Outside of this range, the beads can be non-spherical, and are characterized by a rough surface having pits and protrusions” (*id.* at 7). Appellants contend that the Jones Declaration teaches that “the lyophilized mannitol beads of the present invention demonstrate a high degree of crystallinity” (*id.*). Appellants contend that the Jones Declaration teaches that “the lyophilized mannitol beads of the present invention are surprisingly uniform, as compared to beads with a similar % w/v trehalose” (*id.* at 8).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s finding that Park and Trembl render claim 1 obvious?

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<sup>5</sup> Declaration of Dr. Martin Jones, filed July 12, 2007.

*Findings of Fact*

3. Park teaches “an instant reagent for PCR(hereinafter referred to as ‘PCR reagent’) of the present invention is prepared by freeze-drying a conventional aqueous reaction mixture which consists of a reaction buffer,  $MgCl_2$ , dNTPs and a DNA polymerase” (Park, col. 3, ll. 3-7).

4. Park teaches that the “PCR reagent of the invention preferably comprises a stabilizer such as . . . polyol (e.g., glycerol, glucose, mannitol, galacitol, glucitol and sorbitol), most preferably, polyol, since polyol is determined to play a role as a sedimenting agent” (Park, col. 3, ll. 23-29).

5. Park teaches “PCR products amplified by the lyophilized reaction mixtures containing 20 mM of . . . mannitol. . . [I]t was clearly demonstrated that polyols improved heat stability of the lyophilized PCR mixture.” (Park, col. 5, ll. 60-67.)

6. Treml teaches “a homogeneous solution of glass-forming filler material, biological reagent, and water which provides a viscosity such that controlled droplets can be dispensed on an inert cryogenic surface and vacuum dried so as to form a spherical biological reagent that is stable at room temperature and soluble in water” (Treml, col. 3, ll. 41-45).

7. Treml teaches that

The preferred biological reagents of the present invention are enzymes and cofactors that provide a reagent system to detect, amplify, modify or sequence nucleic acids. Such enzymes include but are not limited to DNA polymerases (e.g., Klenow), T7 DNA polymerase or various thermostable DNA polymerases such as Taq DNA polymerase; AMV or murine reverse transcriptase, T4 DNA ligase, T7, T3, SP6 RNA polymerase, and restriction enzymes. Cofactors include nucleotides, oligonucleotides,

DNA, RNA, required salts for enzyme activity (e.g., magnesium, potassium and sodium), and salts required for buffer capacity. Buffer salts provide a proper pH range and aid stability. Some buffers which may be used include Tris pH 7.6-8.3.

(TremI, col. 7, ll. 23-35.)

8. TremI teaches that, “[p]referably, the second carbohydrate is at least one of the following carbohydrates: . . . sorbitol” (TremI, col. 5, ll. 28-30).

9. TremI teaches that the “high molecular weight polymer concentration can be between 5% to 25% (weight\volume) of the reagent preparation but is preferably 12.5% to 15%. The second carbohydrate is 5% to 15% (w/v).” (TremI, col. 5, ll. 49-52.)

10. The Examiner finds that the “range disclosed by TremI et al. would be about 45% (w/w)” (Ans. 6).

11. The Specification teaches one embodiment where “mannitol is present in the lyophilized bead in a weight percentage of between 40% and 75% (w/w)” (Spec. 11, ll. 26-27).

#### *Principles of Law*

“It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification.” *In re Sneed*, 710 F.2d 1544, 1548 (Fed. Cir. 1983).

“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). “If a person of ordinary skill can implement a predictable variation, § 103 likely bars its



patentability.” *Id.* at 417. Moreover, an “[e]xpress suggestion to substitute one equivalent for another need not be present to render such substitution obvious.” *In re Fout*, 675 F.2d 297, 301 (CCPA 1982). As noted by the Court in *KSR*, “[a] person of ordinary skill is also a person of ordinary creativity, not an automaton.” 550 U.S. at 421.

### *Analysis*

#### *Claim Interpretation*

Claim interpretation is at the heart of patent examination because before a claim is properly interpreted, its scope can not be compared to the prior art. In this case, Appellants challenge the Examiner’s interpretation of two different claim terms, “about 53%” and “substantially spherical.”

#### *“about 53%”*

Appellants contend that to “re-interpret a range of ‘between 53% and 75%’<sup>6</sup> to mean ‘between 42% and 86%’, as the Examiner has now done, completely contravenes the clear meaning of the affected claims. Nor does such a reinterpretation have any basis in the Applicant’s specification” (Reply Br. 3). Appellants contend that “Trem1 teaches away from the present invention by disclosing compositions having at most 40% (w/w) of a carbohydrate, a carbohydrate composition that is substantially *below* the lowest claimed mannitol composition of 53% (w/w)” (App. Br. 6).

During prosecution, claim terms are given their broadest reasonable interpretation as they would be understood by persons of ordinary skill in the

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<sup>6</sup> The claims as presented for appeal state “between about 53% and about 75% (w/w),” include the modifier “about” (*see* Reply to Notice of Non-Compliant Appeal Brief 3, filed June 29, 2009).

art in the light of the Specification. Therefore, we first turn to the Specification to determine whether the meaning of the phrase “about 53%” should be limited as argued by Appellants. Appellants do not identify any portion of the Specification which specifically defines the term “about 53%.”

The Specification teaches one embodiment where “mannitol is present in the lyophilized bead in a weight percentage of between 40% and 75% (w/w)” (Spec. 11, ll. 26-27; FF 11). Thus, the Specification recognizes that mannitol, in an amount of 40% (w/w) is not too low an amount of excipient to permit the material to “coalesce to form a bead-like shape” (Spec. 11, ll. 19-20).

The Examiner finds that the “% taught by prior art Tremblé et al., 45% falls within the lower limit of the range claimed by applicant” (Ans. 7).

We are persuaded that the Examiner has the better position. “[D]uring patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.” *In re Zletz*, 893 F.2d 319, 322 (Fed. Cir. 1989). We agree with the Examiner that “about 53%” is reasonably interpreted as encompassing 45% (see FF 10; Reply Br. 2).

In determining how far beyond the claimed range the term “about” extends the claim, “[w]e must focus ... on the criticality of the [numerical limitation] to the invention.” *Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd.*, 476 F.3d 1321, 1327 (Fed. Cir. 2007). Extending the lower limit of the range based on the “about 53%” language to encompass 45% is consistent with the usage in Appellants’ Specification, which teaches that

mannitol values of 40% will result in functional beads (FF 11). This is particularly reasonable during the course patent prosecution before issuance, where claims may be amended to improve clarity and address uncertain scope.

*“substantially spherical”*

Appellants contend that “the “substantially spherical nature of the beads is inherent to the use of mannitol in the claimed range. Outside of this range, the beads can be non-spherical, and are characterized by a rough surface having pits and protrusions” (App. Br. 7).

We again turn to the Specification to determine whether the meaning of the phrase “substantially spherical” should be limited as argued by Appellants. Appellants do not identify any portion of the Specification which specifically defines the term “substantially spherical.”

The Specification teaches that a “‘bead’ as used herein, refers to a small, often round piece of material. A bead can have a spherical as well as a nearly spherical, *e.g.*, elliptical shape” (Spec. 7, ll. 10-11; FF 1). The Specification teaches that “[e]xemplary shapes include spherical, near spherical, elliptical or round structures” (Spec. 10, ll. 26-27; FF 2).

The Examiner finds that the “lyophilized beads taught by Park and Trembl et al. will necessarily meet the newly added limitation i.e. they will also be ‘substantially spherical in shape’” (Ans. 8).

We are persuaded that the Examiner has the better position. *See In re Zletz*, 893 F.2d at 322. Trembl expressly teaches “a spherical biological reagent that is stable at room temperature and soluble in water” (Trembl, col. 3, ll. 41-45; FF 6). The Specification imposes no specific limitations on the

phrase “substantially spherical” and is reasonably interpreted as encompassing beads which are “near spherical, elliptical or round” (Spec. 10, ll. 26-27; FF 2) as well as beads with “smooth or slightly roughened surfaces” (Spec. 10, ll. 27-28).

*Obviousness*

Park teaches lyophilized PCR reagent mixtures which comprise thermally stable enzymes such as polymerases (FF 3) and polyol stabilizers such as mannitol and sorbitol (FF 4). Park teaches that “it was clearly demonstrated that polyols improved heat stability of the lyophilized PCR mixture.” (Park, col. 5, ll. 60-67; FF 5.)

Treml teaches spherical beads for biological reactions (FF 6) which may include thermally stable enzymes such as polymerases (FF 7) and stabilizers such sorbitol (FF 8). Treml teaches that the sorbitol may compose 5% to 15% (w/v) of the composition (FF 9). The Examiner finds that this range would be “about 45% (w/w)” (FF 10). Appellants contend that “5% (w/v) of carbohydrate is equivalent to about 28% (w/w) and 10% (w/v) is equivalent to about 40% (w/w)” (App. Br. 6, footnote 1).

Appellants do not provide a calculation for the high end of the range for the second carbohydrate disclosed by Treml of 15% w/v of the composition, but this value would reasonably be expected to exceed 40% (w/w) since Appellants find that 10% (w/v) equals 40% (w/w). In addition, Appellants do not dispute the Examiner’s finding that Treml teaches about 45% (w/w) (*see* Reply Br. 2).

Applying the *KSR* standard of obviousness to the findings of fact, we conclude that the person of ordinary creativity would have predictably

modified the Treml beads by substituting mannitol for Treml's sorbitol (FF 8) since Park teaches that these are equivalent polyol stabilizers (FF 4). Further, the ordinary artisan would have reasonably selected the amounts of mannitol suggested by Treml, of 5% (w/v) to 15% (w/v) which the Examiner finds and Appellants do not dispute is equal to about 45% (w/w) (FF 10; Reply Br. 2). Such a combination is merely a "predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417.

Appellants contend that, according to the Jones Declaration, the "substantially spherical nature of the beads is inherent to the use of mannitol in the claimed range. Outside of this range, the beads can be non-spherical, and are characterized by a rough surface having pits and protrusions" (App. Br. 7). Appellants contend that the Jones Declaration teaches that "the lyophilized mannitol beads of the present invention demonstrate a high degree of crystallinity" (*id.*).

We are not persuaded. Treml teaches spherical beads (FF 6) and as reasonably interpreted above, beads with pits or protrusions satisfy the "substantially spherical" requirement of the claims. There is no requirement in claim 1 for any specific level of "crystallinity" (*see* claim 1). "[L]imitations are not to be read into the claims from the specification." *In re Van Geuns*, 988 F.2d 1181, 1184 (Fed. Cir. 1993) (citing *In re Zletz*, 893 F.2d at 321).

#### *Unexpected results*

Appellants assert that Dr. Jones identifies unexpected results, specifically contending that in "paragraph 6 of the Jones declaration, Dr. Jones declares that the use of mannitol in the claimed range, rather than

other saccharides or oligosaccharides, provides lyophilized beads that are reproducibly spherical” (App. Br. 7). Appellants contend that the “substantially spherical nature of the beads is inherent to the use of mannitol in the claimed range. Outside of this range, the beads can be non-spherical, and are characterized by a rough surface having pits and protrusions” (App. Br. 7). Appellants contend that in “paragraph 8 of the Jones declaration (shown below in paragraph 4 of the Evidence Appendix), Dr. Jones declares that the surprising nature of the lyophilized beads of the present invention is also exemplified by the reproducibility and homogeneity of the size of the lyophilized beads” (*id.*).

We have considered the Declaration of Dr. Jones, but are not persuaded. The asserted unexpected results are not commensurate in scope with the claims, which are not limited to either “53% to 75% mannitol” or to perfectly spherical beads without pits or protrusions. *See In re Harris*, 409 F.3d 1339, 1344 (Fed. Cir. 2005) (Unexpected results must also be “commensurate in scope with the degree of protection sought by the claimed subject matter.”)

We also note that the spherical nature of the beads was not compared to the melezitose beads of Trem1, the closest prior art, but rather to trehalose containing beads (*see* Jones Dec. 4 ¶ 6). *See In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) (“[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.”).

*Conclusion of Law*

The evidence of record supports the Examiner's finding that Park and Trembl render claim 1 obvious.

*C. 35 U.S.C. § 103(a) over Park, Trembl, and Kellogg*

The Examiner finds it obvious "to incorporate the Taq DNA Polymerase coupled to neutralizing TaqStartAntibody™, of Kellogg et al. in the product of Park et. al. and Trembl et al." (Ans. 10.)

The Examiner provides sound fact-based reasoning for combining Kellogg with Park and Trembl (*see id.*). We adopt the fact finding and analysis of the Examiner as our own. Appellants argue the underlying obviousness rejection over Park and Trembl, but Appellants do not identify any material defect in the Examiner's reasoning for combining Kellogg with Park and Trembl. Since Appellants only argue the underlying rejection of Park and Trembl which we affirmed above, we affirm this rejection for the reasons stated by the Examiner.

*D. 35 U.S.C. § 103(a) over Park, Trembl, and Shively*

The Examiner finds it obvious "to incorporate the buffer of Shively et al. in the product of Park et al. and Trembl et al." (Ans. 11.)

The Examiner provides sound fact-based reasoning for combining Shively with Park and Trembl (*see id.*). We adopt the fact finding and analysis of the Examiner as our own. Appellants argue the underlying obviousness rejection over Park and Trembl, but Appellants do not identify any material defect in the Examiner's reasoning for combining Shively with Park and Trembl. Since Appellants only argue the underlying rejection of

Park and Trembl which we affirmed above, we affirm this rejection for the reasons stated by the Examiner.

#### SUMMARY

In summary, we reverse the rejection of claims 1-10, 12, 45-48, and 50-53 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

We affirm the rejection of claim 1 under 35 U.S.C. § 103(a) as obvious over Park and Trembl. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 2-7, 10, 12, 45-48, 52, 53, 63, and 64 as these claims were not argued separately.

We affirm the rejection of claims 8 and 50 under 35 U.S.C. § 103(a) as obvious over Park, Trembl, and Kellogg.

We affirm the rejection of claims 9 and 51 under 35 U.S.C. § 103(a) as obvious over Park, Trembl, and Shively.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

#### AFFIRMED

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